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(71) Applicant *(for all designated States except US)*: **ALGOS THERAPEUTICS, INC.** [US/US]; 1360 Energy Park Drive, Suite 300, St. Paul, MN 55108 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **SHUSTER, Samuel, J.** [US/US]; 6712 Apache Road, Edina, MN 55439 (US). **ARVIDSSON, Ulf, N., G.** [SE/SE]; Gardstigen 4, S-Lidingo (SE). **STONE, Laura, S.** [CA/US]; 2242 Nevada Avenue South, Apt. 19, St. Louis Park, MN 55426 (US). **ZHANG, Hong-Yan** [CN/SE]; Sevensvagen 4, S-Sundbyberg (SE). **HART, Lucy, Vulchanova** [BG/US]; 2117 Niles Avenue, St. Paul, MN 55116 (US).

(74) Agent: **ELLINGER, Mark, S.**; Fish & Richardson P.C., P.A., Suite 3300, 60 South Sixth Street, Minneapolis, MN 55402-1104 (US).

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS AND MATERIALS FOR MODULATING TRPM2

(57) Abstract: The invention relates to antisense oligonucleotides, compositions and methods useful for modulating the expression of TRPM2. The compositions comprise antisense oligonucleotides, particularly antisense oligonucleotides targeted to nucleic acids encoding TRPM2.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/38685

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07H 21/04; A61K 48/00; C12N 15/85,15/86
US CL : 536/24.5; 514/44; 435/325

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 536/24.5; 514/44; 435/325

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X — Y	US 5,614,617 a (COOK et al.) 25 March 1997 (25.03.1997), see entire document, particularly SEQ ID NO 18.	1,2,4-8,17 — 13-16
Y	US 2002/0081658 A1 (CURTIS) 27 June 2002 (27.06.2002), see entire document	13-16

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
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Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (703) 305-3230

Authorized officer
Tracy Vivlemore

Telephone No. 571-272-1600

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INTERNATIONAL SEARCH REPORT

Interna[redacted]l application No.
PCT/US03/38685

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-8 and 13-17

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US03/38685

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

Group I Claims 1-8 and 13-17, drawn to an isolated antisense oligonucleotide of SEQ ID NO 1 which inhibits TRPM2, a nucleic acid that encodes a transcript that hybridizes with TRP2 mRNA and the first method of using antisense oligonucleotides to decrease production of TRPM2
Group II Claims 9-11, drawn to an isolated oligonucleotide of SEQ ID NO 2
Groups III-XV Claim 12, drawn to multiple oligonucleotides of SEQ ID NO 3-SEQ ID NO 15
Group XVI Claim 18, drawn to a method of modulating pain in a mammal
Group XVII Claims 19-22, drawn to a method to identify compounds to modulate pain in a mammal
Group XVIII Claim 23, drawn to a second method to identify compounds to modulate pain in a mammal
Group XIX Claims 24-26, drawn to a third method to identify compounds to modulate pain in a mammal
Group XX Claims 27-28, drawn to a fourth method to identify compounds to modulate pain in a mammal

The inventions listed as Groups I-XV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: According to the guidelines in Section (f)(i)(a) of Annex B of the PCT Administrative Instructions, the special technical feature as defined by PCT Rule 13.2 shall be considered to be met when all the alternatives of a Markush-group are of similar nature. For chemical alternatives, such as the claimed oligonucleotide sequences, the Markush groups shall be regarded as being of similar nature when:
(A) all alternatives have a common property or activity and
(B)(1) a common structure is present, i.e., a significant structure is shared by all of the alternatives or
(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to an art recognized class of compounds in the art to which the invention pertains.

The instant oligonucleotide sequences are considered to be each separate inventions for the following reasons:

The sequences do not meet the criteria of (B)(1), common structure present. The oligonucleotide sequences of the instant application are not disclosed as sharing a common structure. Although the oligonucletide sequences of the instant application are all termed antisense nucleic acids, each sequence has a unique nucleotide structure and hybridizes to a unique complementary sequence. Each member of the class cannot be substituted, one for the other, with the expectation that the same intended result would be achieved. Therefore, although the instant oligonucleotide sequences are characterized as antisense nucleic acids, the sequences do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure. Accordingly, unity of invention between the oligonucleotide sequences of the instant application is lacking and each oligonucleotide sequence claimed is considered to constitute a special technical feature.

As an oligonucleotide sequence is recited in the first claimed invention, applicants will obtain a search of the first sequence listed in the claims, SEQ ID NO 1. For every other sequence applicants wish to have searched, applicants need to elect the sequence and pay an additional fee.

If the sequences are recited in the second or subsequent claimed invention, applicants will need to elect the group and pay the fee to obtain a search of the first sequence listed in the claims encompassed by the second or subsequent group. For every other sequence in the second/subsequent group that applicants wish to have searched, applicants need to elect the sequence and pay an additional fee.

The special technical feature of group I is considered to be an antisense olignonucleotides against TRPM2 comprising SEQ ID NO 1, a nucleic acid that encodes an antisense against TRPM2 and a method of decreasing production of TRPM2.

The special technical feature of group II is considered to be a second antisense olignonucleotides against TRPM2 comprising SEQ ID NO 2.

The special technical feature of groups III-XV is considered to be olignonucleotides comprising SEQ ID NOS 3-15.

The special technical feature of group XVI is considered to be a method of modulating pain in a mammal.

The special technical feature of group XVII is considered to be a method for identifying compounds to modulate pain in a mammal.

The special technical feature of group XVIII is considered to be a second method for identifying compounds to modulate pain in a mammal.

The special technical feature of group XIX is considered to be a third method for identifying compounds to modulate pain in a mammal.

The special technical feature of group XX is considered to be a fourth method for identifying compounds to modulate pain in a mammal.